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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LANDSMAN, ROBERT S

ART UNIT PAPER NUMBER

1647

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/083,446

Applicant(s)

BAUER ET AL.

Examiner

Robert Landsman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 55-65 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 55-65 is/are rejected.
- 7) ☒ Claim(s) 60 and 61 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Formal Matters

A. Claims 55-65 are pending in the application and were subject to restriction in Paper No. 5, mailed 1/29/03. In Paper No. 6, filed 2/28/03, Applicants elected Group V, with traverse and stated that election of the five Groups simultaneously would not impose an undue search burden. This argument has been considered. This application is drawn to cultured stem cells which have been grown in the presence of one of 44 different IL-3 mutants. Searching all of these SEQ ID NOs is, in itself, an undue burden. However, the Examiner noticed that these SEQ ID NOs and claim limitations are found in numerous parents (e.g. 6,436,387; 6,361,9776,057,133) and are recited almost identically. Therefore, the Examiner has decided to withdraw the restriction requirement and examine all of the claims.

2. Title

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title is drawn to methods of expanding stem cells, whereas the claims themselves are drawn to stem cells alone.

3 Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 60, 61 and 64 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are confusing since it is not clear what is meant by the phrase "wherein is R2 is R1" and "wherein is R2." Claim 64 is rejected since it depends from rejected claim 60/

4. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

A. Claims 55-65 are rejected under 35 U.S.C. 102(e) as being anticipated by Hoffman et al. (U.S. Patent 5,409,825). The present claims recite cultured stem cells obtained from a method of ex-vivo expansion of stem cells comprising culturing said cells with a mutant IL-3/hematopoietic growth factor chimera. Hoffman et al., in which the parent case receives priority to April 9, 1991, teach a method of supporting hematopoietic progenitor (i.e. stem) cells by using MGF in addition to an IL-3/GM-CSF fusion protein (column 1, lines 62-68) as well as the cells to be supported (column 5, lines 22-36). Therefore, the stem cells of Hoffman et al. have been obtained using a medium comprising an IL-3/GM-CSF fusion protein. Though the IL-3 of Hoffman et al. is not a mutant IL-3 as described by the present claims, in absence of evidence to the contrary, the stem cells would be identical.

B. Claims 55-65 are rejected under 35 U.S.C. 102(e) as being anticipated by Emerson et al. (U.S. Patent 6,326,198). The present claims recite cultured stem cells obtained from a method of ex-vivo expansion of stem cells comprising culturing said cells with a mutant IL-3/hematopoietic growth factor chimera. Emerson et al. teach stem cells which have been produced/maintained in the presence of IL-3 and GM-CSF, in the presence or absence of IL-6 (column 6, lines 64-67). See also columns 27-28 regarding the use of IL-3 and a growth factor. Though the IL-3 of Emerson et al. is not a mutant IL-3 as described by the present claims, in absence of evidence to the contrary, the stem cells would be identical.

Note:

The following limitations were recited in previous US Patents which are parents of the instant case. However, these limitations are not recited in the current claims. Therefore, Applicants are requested to recite these limitations in the claims, or to provide an explanation as to why these limitations should not be included. It is believed that these limitations were required to overcome prior art and scope of enablement rejections:

(a) with the proviso that no more than one of the amino acids at positions 63, 82, 87, 98, 112, and 121 are different from the corresponding amino acids in native human interleukin-3; and

(b) wherein said modified human interleukin-3 (hIL-3) amino acid sequence has increased activity, relative to native human interleukin-3, in at least one assay selected from the group consisting of: AML cell proliferation, TF-1 cell proliferation and Methylcellulose assay; R.sub.2 is a hematopoietic growth factor; and L is a linker capable of Linking R.sub.1 to R.sub.2 ; and (b) harvesting said cultured stem cells.

(c) provided that the residues corresponding to positions 101 or 116 are not Ala or Val, respectively and wherein a polypeptide having only the sequence of said mutant human interleukin-3 polypeptide R.sub.1 has at least three times greater activity than native human interleukin-3, in at least one assay selected from the group consisting of: AML cell proliferation, TF-1 cell proliferation and Methylcellulose assay;

5. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

A. Claims 55-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman et al. in view of Curtis et al. (WO 91/02754). The present claims recite cultured stem cells obtained from a method of ex-vivo expansion of stem cells comprising culturing said cells with a mutant IL-3/hematopoietic growth factor chimera.

The teachings of Hoffman et al. are discussed in the above rejection under 35 USC 102. Though Hoffman et al. do specifically teach the use of an IL-3/GM-CSF fusion protein, it appears that they do not

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use this fusion protein alone. Though Hoffman et al. still meet the limitations of the claims under 35 USC 103, further motivation for using the fusion protein alone (i.e. in the absence of MGF) is provided here.

Curtis et al. do teach that a fusion protein comprising a IL-3/GM-CSF fusion protein and that this protein is more biologically active than either of the two proteins alone (Abstract). Therefore, it would have been obvious to substitute the fusion protein of Curtis et al. for the combination of fusion protein and MGF of Hoffman et al. since it would be expected that the fusion protein of Curtis would have had desirable effects on the stem cells of Emerson (page 1, line 31 – page 2, line 3 of Curtis et al.). Given this teaching by Curtis that simultaneous administration of IL-3/GM-CSF was more effective than either IL-3 or GM-CSF alone, it would have been obvious to have used this fusion protein since this would guarantee simultaneous administration of these proteins to progenitor (i.e. stem) cell and would not require the addition of other hematopoietic growth factors.

B. Claims 55-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Emerson et al. in view of Curtis et al. (WO 91/02754). The present claims recite cultured stem cells obtained from a method of ex-vivo expansion of stem cells comprising culturing said cells with a mutant IL-3/hematopoietic growth factor chimera.

The teachings of Emerson are discussed in the above rejection under 35 USC 102. Emerson et al. do not specifically teach the use of an IL-3/GM-CSF fusion protein. However, Curtis et al. do teach that a fusion protein comprising a IL-3/GM-CSF fusion protein and that this protein is more biologically active than either of the two proteins alone (Abstract). Therefore, it would have been obvious to substitute the fusion protein of Curtis et al. for the individual IL-3 and GM-CSF proteins of Emerson et al. since it would be expected that the fusion protein of Curtis would have had desirable effects on the stem cells of Emerson (page 1, line 31 – page 2, line 3 of Curtis et al.). Given this teaching by Curtis that simultaneous administration of IL-3/GM-CSF was more effective than either IL-3 or GM-CSF alone, it would have been obvious to have used this fusion protein since this would guarantee simultaneous administration of these proteins to progenitor (i.e. stem) cell.

6. Conclusion

A. No claim is allowable

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Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
May 19, 2003


ROBERT LANDSMAN
PATENT EXAMINER